ST

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,943	10/01/2003	Lawrence M. Nelson	4239-64790	1005

36218 7590 01/09/2006

KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET, SUITE #1600
ONE WORLD TRADE CENTER
PORTLAND, OR 97204-2988

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/677,943	**Applicant(s)** NELSON ET AL.	
	Examiner Michael Szperka	**Art Unit** 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-21,24,25,29 and 31-38* is/are pending in the application.

4a) Of the above claim(s) *7-21,24,25,29 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date *1/16/04,6/27/05*.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received October 20, 2005 is acknowledged.

Claims 1-5, have been amended.

Claims 32-38 have been added.

Claims 6, 22, 23, 26-28, and 30 are canceled.

Claims 1-5, 7-21, 24, 25, 29, and 31-38 are pending in the instant application.

Applicant's election without traverse of Group I, claims 1-5 and new claims 32-38, drawn to MATER polypeptides, and the species of ATP/GTP binding domain, in the reply filed on October 20, 2005 is acknowledged. The search of the prior art has been extended beyond the elected species.

Claims 7-21, 24, 25, 29, and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in the reply filed on October 20, 2005.

Claims 1-5 and 32-38 are under examination as they read on MATER and variant MATER polypeptides.

Applicant is reminded to update the status of all applications disclosed in the instant specification, especially those to which priority has been claimed in the first line of the specification.

Information Disclosure Statement

2. Applicant's IDS forms received January 16, 2004 and June 27, 2005 are acknowledged and have been considered.

Priority

3. Applicant's priority claims to US provisional application 60/241,510, filed October 18, 2000, to PCT/US01/10981 filed April 4, 2001 and to PCT/US02/09776 filed March 29, 2002 are acknowledged. The provisional application does not disclose the full-length polypeptide or polynucleotide sequence of human MATER (i.e., it does not disclose SEQ ID NO:23 and SEQ ID NO:24), and PCT/US01/10981 does not appear to disclose support for the various recited locations of putative functional domains, such as a PAAD-DAPIN domain, within the sequence of MATER. As such, it appears that the proper priority date for examination of the instant claims in view of prior art is as follows:

October 18, 2000 -	Claim 37
April 4, 2001 -	Claims 1, 32, and 38
March 29, 2002 -	Claims 2-5, and 33-36

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Examples of such code can be found in lines 11-15 of page 38.

The specification is also objected to because "oxireductase" in line 34 of page 38 should be oxidoreductase as is recited in the instant claims.

The title is also objected to because it does not clearly identify the claimed subject material. A possible title that is more descriptive is "Polypeptides of MATER, a Maternal Antigen That Embryos Require", or something similar that specifies the subject mater of the instant claims.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-5 and 33-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, these claims recite domains

consisting of amino acids X to Y and refer back to a base claim that recites many potential sequences. As such, the identity and sequence of the amino acid string recited in these dependent claims is not clear. Amendment of the claims to indicate that the recited domains consist of amino acids X to Y of SEQ ID NO:24, for example, would be one way to overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5 and 32-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated MATER polypeptide consisting of SEQ ID NO:24 or encoded by SEQ ID NO:23, does not reasonably provide enablement for polypeptide fragments comprising SEQ ID NO:2 or SEQ ID NO:4, for variant MATER polypeptides, or for polypeptides that hybridize to SEQ ID NO:1, SEQ ID NO:3,or SEQ ID NO:23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has claimed a genus of polypeptides consisting of the full length MATER polypeptide (SEQ ID NO:24, encoded by SEQ ID NO:23), MATER fragments (SEQ ID NO:2,encoded by SEQ ID NO:1, and SEQ ID NO:4, encoded by SEQ ID

NO:3), and variant MATER polypeptides and polypeptide fragments that contain at least 1 amino acid that is different from the sequence disclosed of wild type human MATER.

It was known in the prior art that MATER expression was important for the development of embryos beyond the two cell stage, although the exact function of MATER was not known (see the entirety of Tong et al., of record as C25 on the IDS received 1/16/04, particularly page 285, the first paragraph of the right column). Tong et al. hypothesized that MATER functions as a ribonuclease inhibitor due to the identification of a putative ribonuclease inhibitor domain through homology analysis (see particularly page 285, the first paragraph of the right column and figure 4). The instant specification indicates many potential roles for MATER in embryogenesis (see from line 10 of page 29 to line 10 of page 30) and argues against the ability of MATER to function as a ribonuclease inhibitor (see particularly lines 16-18 of page 29), but guidance as to which of the proposed functions are required to support embryogenesis is not clear. Note that the claimed polypeptides are not recited as having any function in embryogenesis, and that claims which do contain functional language indicate that the claimed polypeptide lacks the recited functionality.

Applicant has claimed MATER polypeptide fragments as well as variant MATER polypeptide sequences, with variants defined as having one or more amino acids changed from the wild type MATER sequence (see particularly lines 18-30 of page 15 and lines 14-28 of page 20). Note that sequences that hybridize to SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:23 can contain nucleotide mismatches, and as such they encode variant MATER polypeptides. The specification indicates that MATER sequence variants are possible and indicates putative structural domains that are found within the full length MATER sequence of SEQ ID NO:24 (see particularly lines 4-15 of page 23 and Figure 14B). These regions were determined based upon homology with proteins of known function (see particularly lines 9-35 of page 38), but it does not appear that these domains were experimentally verified to have predicted function, such as the ability to bind ATP or to have oxidoreductase activity. The specification does not appear to disclose which, if any, of the computationally identified domains are important for the survival of the embryo beyond the two cell stage, the only property that can be ascribed to MATER with any certainty. Indeed, it is not clear that the disclosed sequence fragments of full-length MATER (i.e. SEQ ID NO:1-4) are sufficient for the defined functional property of being important for the survival of the embryo beyond the two cell stage, and no data concerning the biological activities MATER fragments, or the function and biological properties of variant MATER polypeptides, appear to be included with the specification.

Skolnick et al. (Trends in Biotechnology, 18:34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36).

The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly Reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323). Applicant discloses that the putative domains identified within the polypeptide of SEQ ID NO:24 have been identified through homology, and applicant appears to speculate that such domains are important for function. However, neither the specification nor the prior art appear to clearly indicate what structural region(s) of MATER are essential for maintenance of its biological function in promoting embryogenesis beyond the two cell stage since all that appears to be known is that when MATER polypeptide is missing in a knockout mouse, embryos do not survive past the two cell stage. Applicant has speculated that the presence of leucine rich repeats (LLR) in MATER indicates that these computationally identified LLR are important for protein-protein interactions between MATER and other cellular proteins (see particularly lines 29-32 of page 38). The prior art does recognize that LLR are important for interactions with other proteins, but the presence of an LRR in a particular protein does not provide any guidance concerning the function of the LRR containing protein or the identity of other proteins that interact with the LRR containing protein (Kobe et al., of record as C12 on the IDS received 1/16/04, see entire document, particularly the second paragraph of page 7 and the second complete paragraph of page 9). As such, it is not clear what domain(s) of MATER are important for its disclosed biological activity of promoting embryogenesis beyond the two cell stage, and it is not clear what changes, if any, can be made to its sequence that maintain the disclosed function.

All variant MATER polypeptides are recited as being specifically bound by MATER-protein specific binding agents. The specification provides non-limiting examples of such agents as anti-MATER antibodies or as soluble receptors for MATER (see particularly lines 25-29 of page 18). As has been discussed previously, the specification does not disclose the identity of any receptors or other polypeptides that bind MATER, and the identification of domains within MATER based on homology also does not identify polypeptides that may act as receptors for MATER. The specification does disclose antibodies that bind MATER (see particularly the paragraph that spans pages 18 and 19, and Example 17). The utilities disclosed by the instant specification concerning anti-MATER antibodies include their use to quantitatively and semi-quantitatively detect the presence of MATER antigen in biological samples obtained from human patients via immunoassays (see particularly lines 29-31 of page 51 and Example 19). As such, anti-MATER antibodies must be capable of binding to the native, wild type sequence of MATER that is found in patients. Colman et al. teaches that even single amino acid changes in an antigen can abolish the binding of an antibody to the antigen (Research in Immunology, (1994) 145:33-36, see entire document, particularly the right column of page 33). Therefore, variant MATER polypeptides with one or more sequence changes may not be bound by the anti-MATER antibodies disclosed in the instant specification. Note that the specification does not appear to teach the specific alterations to the wild type sequence of MATER that maintain binding with antibodies or other ligands that recognize wild type MATER, or conversely, which changes cannot be made to the sequence of MATER without destroying reactivity.

Therefore, given that neither the specification nor the prior art indicate the precise role played by MATER in embryogenesis, that neither the specification nor the prior art appear to indicate which domain(s) of MATER are important for its biological activity, that assignment of function based upon homology is often inaccurate and hence unpredictable as evidenced by Skolnick et al. and Whisstock et al., the teachings of Kobe et al. which indicate that even if a domain is identified in a protein, the presence of this domain does not lead to knowledge of the protein's function or to knowledge of the ligands that bind said protein, the apparent lack of data concerning confirmation that the domains identified by applicant in MATER via homology-based computational methods are functional and have the appropriate activity, such as ATP binding or oxidoreductase activity, the apparent lack of data concerning the ability of fragments of MATER, such as SEQ IDS NO:2 or SEQ ID NO:4, to play a role in embryogenesis, the fact that none of the recited MATER variants are required to have any functional activity, and the fact that it is not clear that a variant MATER polypeptide can be bound by disclosed MATER-protein specific binding agents, a skilled artisan would not expect any polypeptide sharing less than 100% identity with the full length sequence of MATER (SEQ ID NO:24) to retain the functional properties of promoting embryo survival beyond the two cell stage. As such, a skilled artisan would be unable to make and use the full breadth of applicant's claimed polypeptide sequences without first conducting additional research.

7. Claims 1-5 and 32-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a polypeptide consisting of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:24.

Applicant is not in possession of isolated variant MATER polypeptide sequences.

Applicant has broadly claimed polypeptide sequences that are variants of disclosed sequences, wherein a variant has at least one, but potentially more, sequence differences from the disclosed polypeptide sequences (see particularly form lines 18-25 of page 15 and lines 14-28 of page 20) and has the recited property of being bound by a MATER-protein specific binding agent (see also lines 25-29 of page 18). Note that the recited polynucleotides that hybridize can contain sequence variations, and hence they encode variant MATER polypeptides. Binding agents are disclosed as including antibodies and soluble receptors, but the identity of such receptors does not appear to be disclosed by the instant specification. Kobe et al. teach that even if a protein is predicted to contain a particular structural domain, the presence of this domain does not provide guidance to the identity of other polypeptides that bind said protein (of record as reference C12, see entire document, particularly the second paragraph of page 7 and the second complete paragraph of page 9). The specification also discloses anti-MATER antibodies and teaches their use in quantitatively and semi-quantitatively detecting the presence of MATER antigen in biological samples obtained from human patients via immunoassays (see particularly lines 29-31 of page 51 and Example 19). As such, anti-MATER antibodies must be capable of binding to the native, wild type sequence of MATER that is found in patients. Colman et al. teaches that even single amino acid changes in an antigen can abolish the binding of an antibody to the antigen (Research in Immunology, (1994) 145:33-36, see entire document, particularly the right column of page 33). Therefore, variant MATER polypeptides with one or more sequence changes may not be bound by the anti-MATER antibodies disclosed in the instant specification.

Applicant has recited various regions of MATER in which mutations from the wild type sequence of MATER can be located. These regions were identified using computer based homology programs (see particularly lines 9-35 of page 38), but it does not appear that these domains were experimentally verified to have predicted function, such as the ability to bind ATP or to have oxidoreductase activity. The specification does not appear to disclose which, if any, of the computationally identified domains are important for the survival of the embryo beyond the two cell stage, the only property that can be ascribed to MATER with any certainty. Indeed, it is not clear that the disclosed sequence fragments of full-length MATER (i.e. SEQ ID NO:1-4) are sufficient for the defined functional property of being important for the survival of the embryo beyond the two cell stage, and no data concerning the biological activities of MATER fragments, or the function and biological properties of variant MATER polypeptides, appear to be disclosed by the specification.

Skolnick et al. (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly Reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323). Applicant discloses that the putative domains identified within the polypeptide of SEQ ID NO:24 have been identified through homology, and applicant appears to speculate that such domains are important for function. However, neither the specification nor the prior art appear to clearly indicate what structural region(s) of MATER are essential for maintenance of its biological function in embryogenesis beyond the two cell stage since all that appears to be known is that when MATER polypeptide is missing in a knockout mouse, embryos do not survive past the two cell stage. As such, it does not appear that the specification discloses the structure of MATER that must be maintained to ensure the survival of an embryo past the two-cell stage or conversely what structures can be mutated without impairing embryo survival.

Therefore, given that variant MATER polypeptides must be bound by antibodies that recognize wild-type MATER in patient samples, that Colman teaches that even single amino acid differences in an antigen can abolish antibody-antigen binding, that the identification of putative domains in a molecule does not identify the ligands that bind said molecule as taught by Kobe et al., that the identification of the domains within MATER to be mutated were identified using a computer based homology approach that can often give incorrect assignments as taught by Skolnick et al. and Whisstock et al., that the specification does not appear to teach the specific sequence of any MATER variant, and that based upon the specification it is unclear what mutation or variants of the sequence of wild type MATER (SEQ ID NO:24) can or cannot be made commensurate with maintenance of the biological activity of MATER in somehow promoting embryogenesis beyond the two cell stage, a skilled artisan would reasonably conclude that applicant was not in possession of the claimed genus encompassing all MATER variant polypeptides. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 2, 32, 33, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Ramkumar et al., US2004/0043452 A1 (see entire document).

Ramkumar et al. disclose the polypeptide sequence of EMBRY-1, as well as sequence fragments and derivatives of EMBRY-1, and teach antibodies that bind EMBRY-1 and its derivatives (see entire document, particularly the abstract and paragraphs 11-16, 19, 59-61, 121, 167-170, 174,175, 177, 181 and claims 1, 2, 11, 56, and 57).

EMBRY-1 is 93.6% similar to SEQ ID NO:24, and as such EMBRY-1 is a variant MATER polypeptide (see enclosed sequence search notes). Note that EMBRY-1 differs from SEQ ID NO:24 in the putative LRR consisting of amino acids 895-918 of SEQ ID NO:24, and that it comprises SEQ ID NO:4 (see sequence search notes). Given that the instant specification does not appear to disclose which residue or residues in the LRR consisting of amino acids 895-918 of SEQ ID NO:24 mediate interactions with at least one protein in a cell, it appears reasonable that mutation of any amino acid in this region creates a variant MATER protein with a differential interaction with at least one protein in a cell and hence claim 33 has been included with this rejection.

Therefore, the prior art anticipates the instant invention

10. No claims are allowable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
January 03, 2006

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600
1/6/05